

FIG.1

ADAMTS-E nucleotide sequence [SEQ ID NO: 1]

CACGCGTCCGACGGCGCGGAGGCCCGGGCGGCGCAGGAGCCCGGTGAT
5 GCTGCGAAGGCTGTGAACAGGGGAGGCGGCACTGTGGGGGCTGCCGGCAGCCGGGG
CTGGGGAGAGACATGTGGACACGTGGCCTCTATGGCTCCCGCCTGCCAGATCCTCCGC
TGGGCCCTCGCCCTGGGGCTGGGCCTCATGTTGAGGTACGCACGCCTTCCGGTCTC
AAGATGAGTTCCTGTCCAGTCTGGAGAGCTATGAGATCGCCTTCCCCACCCGCGTGGAC
CACAAACGGGGCACTGTGGCCTTCTCGCCACCTCCTCCCCGGAGGCGAGCGCCGCGGC
10 ACGGGGGCCACAGCCGAGTCCCGCCTCTTCTACAAAGTGGCCTCGCCAGCACCCACT
TCCTGCTGAACCTGACCCGACGTCCCGTCTACTGGCAGGGGACGTCTCCGTGGAGTA
CTGGACACGGGAGGGCCTGGCCTGGCAGAGGGCGGCCCGGCCCACTGCCTCTACGC
TGGTCACCTGCAGGGCCAGGCCAGCACCTCCCATGTGGCCATCAGCACCTGTGGAGGC
CTGCACGGCCTGATCGTGGCAGACGAGGAAGAGTACCTGATTGAGCCCTGCACGGTG
15 GGCCCAAGGGTTCTCGGAGCCCGGAGGAAAGTGGACCACATGTGGTGTACAAGCGTTC
CTCTCTGCGTCACCCCCACCTGGACACAGCCTGTGGAGTGAGAGATGAGAAACCGTGG
AAAGGGCGGCCATGGTGGCTGCGGACCTTGAAGCCACCGCCTGCCAGGCCCTGGGG
AATGAAACAGAGCGTGGCCAGCCAGGCCTGAAGCGATCGGTACGCCGAGAGCGCTACG
TGGAGACCCTGGTGGTGGCTGACAAGATGATGGTGGCCTATCACGGGCGCGGGATGT
20 GGAGAGTATGTCTCTGGCCATCATGAACATTGTTGCCAACTTTTCCAGGACTCGAGTCT
GGGAAGCACCGTTAACATCCTCGTAACTCGCCTCATCCTGCTCACGGAGGACCAGCCCA
CTCTGGAGATCACCCACCATGCCGGGAAGTCCCTGGACAGCTTCTGTAAGTGGCAGAAA
TCCATCGTGAACCACAGCGGCCATGGCAATGCCATTCCAGAGAACGGTGTGGCTAACCA
TGACACAGCAGTGCTCATCACAGCTATGACATCTGCATCTACAAGAACAACCTGCG
25 GCACACTAGGCCTGGCCCGGTGGGCGGAATGTGTGAGCGCGAGAGAAGCTGCAGCG
TCAATGAGGACATTGGCCTGGCCACAGCGTTACCATTGCCACGAGATCGGGCACACA
TTCGGCATGAACCATGACGGCGTGGGAAACAGCTGTGGGGCCCGTGGTCAGGACCCAG
CCAAGCTCATGGCTGCCACATTACCATGAAGACCAACCCATTCTGTGTGTCATCCTGC
AGCCGTGACTACATACCAGCTTTCTAGACTCGGGCCTGGGGCTCTGCCTGAACAACCG
30 GCCCCCAGACAGGACTTTGTGTACCCGACAGTGGCACCGGGCCAAGCCTACGATGCA
GATGAGCAATGCCGCTTTCAGCATGGAGTCAAATCGCGTCAGTGTAATACGGGGAGGT
CTGCAGCGAGCTGTGGTGTCTGAGCAAGAGCAACCGGTGCATCACCACAGCATCCCG
GCCGCCGAGGGCACGCTGTGCCAGACGCACACCATCGACAAGGGGTGGTGTACAAAC
GGGTCTGTGTCCCTTTGGGTGCGGCCAGAGGGTGTGGACGGAGCCTGGGGGCCGT
35 GGACTCCATGGGGCGACTGCAGCCGGACCTGTGGCGGCGGCGTGTCTCTTCTAGCC
GTCACTGCGACAGCCCCAGGCCAACCATCGGGGGCAAGTACTGTCTGGGTGAGAGAA
CGGGCACCGCTCCTGCAACACGGATGACTGTCCCCTGGCTCCAGGACTTCAGAGAA

EXPRESS MAIL NO. E446402267 US

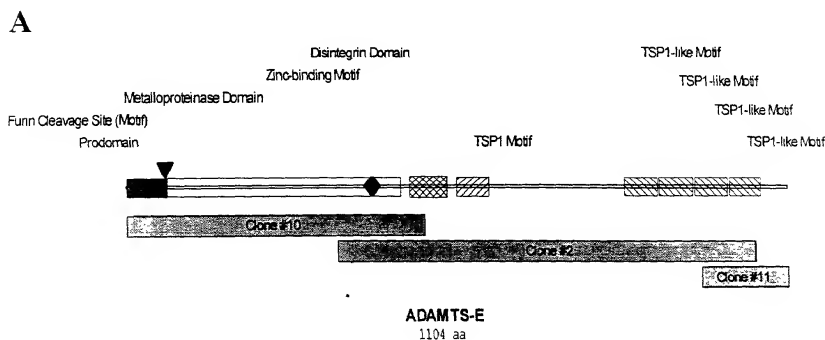
GTGCAGTGTCTGAATTTGACAGCATCCCTTTCCGTGGGAAATTCTACAAGTGAAAAACG
 TACCGGGGAGGGGGCGTGAAGGCCTGCTCGCTCACGTGCCAGCGGAAGGCTTCAACT
 TCTACACGGAGAGGGCGGCAGCCGTGGTGGACGGGACACCCTGCCGTCCAGACACGG
 TGGACATTTGCGTCAGTGGCGAATGCAAGCACGTGGGCTGCGACCGAGTCTCTGGGCTC
 5 CGACCTGCGGGAGGACAAGTGCCGAGTGTGTGGCGGTGACGGCAGTGCCTGCGAGAC
 CATCGAGGGCGTCTTCAGCCCAGCCTCACCTGGGGCCGGGTACGAGGATGTCGTCTGG
 ATTCCCAAAGGCTCCGTCCACATCTTCATCCAGGATCTGAACCTCTCTCAGTCACTTG
 GCCCTGAAGGGAGACCAGGAGTCCCTGCTGCTGGAGGGGCTGCCCGGGACCCCCAG
 CCCCACCGTCTGCCTCTAGCTGGGACCACCTTTCAACTGCGACAGGGGCCAGACCAGG
 10 TCCAGAGCCTCGAAGCCCTGGGACCATTAAATGCATCTCTCATCGTCATGGTGTGGCC
 CGGACCGAGCTGCCTGCCCTCCGCTACCGCTTCAATGCCCCCATCGCCCGTGA CTGCG
 TGCCCCCTTACTCTGGCACTATGCGCCCTGGACCAAGTGTCTGGCCCACTGTGCAGG
 CGGTAGCCAGGTGCAGGCGGTGGAGTGCCGCAACCAGCTGGACAGCTCCGCGGTGCG
 CCCCCACTACTGCAGTGCCACAGCAAGCTGCCCAAAGGCAGCGCGCTGCAACACG
 15 GAGCCTTGCCCTCCAGACTGGGTTGTAGGGAAGTGGTCGCTCTGACGCCGAGCTGCG
 ATGCAGGCGTGCGCAGCCGCTCGGTCTGTGCCAGCGCCGCGTCTCTGCCGCGGAGG
 AGAAGGCGCTGGACGACAGCGCATGCCCGCAGCCGCGCCACCTGTACTGGAGCCT
 GCCACGCCCCACTTGCCCTCCGAGTGGGCGGCCCTCGACTGGTCTGAGTGACCC
 CCAGCTGCGGGCCGGGCCTCCGCCACCGCTGGTCCTTTGCAAGAGCGCAGACCACC
 20 GCGCCACGCTGCCCCCGGCGCACTGCTACCCGCGCGCAAAGCACCAGGCCACCATGC
 GCTGCAACTTGCGCCGCTGCCCCCGGCCGCTGGGTGGCTGGCGAGTGGGGTGAGT
 GCTCTGCACAGTGGCGCTCGGGCAGCGGCAGCGCTCGGTGCGCTGCACCAGGCCACA
 CGGGCCAGGCGTGCACGAGTGCACGGAGGCCCTGCGGCCGCCGACTACCACGCAGC
 AGTGTGAGGCCAAGTGCACAGCCCAACCCCCGGGACGGCCCTGAAGAGTGCAAGG
 25 ATGTGAACAAGTGCCTACTGCCCCCTGGTCTCAAATTTAGTTCTGCAGCCGAGCC
 TACTTCCGCCAGATGTGCTGCAAAACCTGCCAGGGCCACTAGGGGGCGCGCGGCACCC
 GGAGCCACAGCTGGCGGGGTCTCCGCCGCCAGCCCTGCAGCGGGCCGGCCAGAGGG
 GGCCCCGGGGGGGGCGGGAAGTGGGAGGGAAGGGTGAGACGGAGCCGGAAGTTATTT
 ATTTGGAACCCCTGCAGGGCCCTGGCTGGGAGGATCCACCCCAACCTCTGCCCTGCC
 30 GCCCCAGGGGCACCCCGACATCCAGGCCACCCCTCATGTTGCTACAGACCTGCCCT
 GGGGCCACACACTCTGCCAGGAAGCCCTACATCAATAAAGTTCTGTCTTGTGTAGAT
 TTCTAAAAAAAAAAAAAA

FIG 2

ADAMTS-E amino acid sequence [SEQ ID NO: 2]

MAPACQILRWALALGLMFEVTHAFRSQDEFSSLESYEIAFPTRVDHNGALLAFS
PPPPRRQRRTGATAESRLFYKVASPTHFLLNLTRSSRLLAGHVSVEYWTREGLA
5 WQRAARPHCLYAGHLQGGASTSHVAISTCGGLHGLIVADEEEYLIEPLHGGPKGSR
SPEESGPHVVYKRSSLRPHLDTACGVRDEKPWKGRPWWLRTLKPPPARPLGNE
TERGQPGLRKRSVSRERYVETLVVADKMMVAYHGRRDVEQYVLAIMNIVAKLFQDSS
LGSTVNILVTRLILLTEDQPTLEITHHAGKSLDSFCKWQKSIVNHSGHGNAIPENGVA
NHDTAVLITRYDICIYKNKPCGTLGLAPVGGMCERERSCSVNEDIGLATAFTIAHEIG
10 HTFGMNHGDBGVNSCGARGQDPAKLMAAHITMKTNPFWSSCSRDIYTSFLDSGLG
LCLNNRPPRQDFVYPTVAPGQAYDADEQCRFQHGVKSRQCKYGEVCSSELWCLSK
SNRCITNSIPAAEGTLCQTHTIDKGWCYKRVCPFGSRPEGVDGAWGPWTPWGDG
SRTC GGGVSSSRHCDSPRPTIGGKYCLGERRRHRSCNTDDCPPGSQDFREVQC
SEFDSIPFRGKFYKWKTYRGGGVKACSLTCLAEGFNFYTERAAAVDGTPCRPTV
15 DICVSGECKHVGC DRVLGSDLREDKCRVCGGDGSACETIEGVFSPASPGAGYEDV
VWIPKGSVHIFIQDLNLSLSHLALKGDQESLLEGLPGTPQPHRLPLAGTTFQLRQGP
DQVQSLEALGPINASLIVMVLARTELPALRYRFNAPIARDSLPYSWHYAPWTKCSA
QCAGGSQVQAVECRNQLDSSAVAPHYCSAHSKLPKRQACNTEPCPPDWVVG
WSLCSRSCDAGVRSRVSVCRRVSAAEKALDDSA CPQPRPPVLEACHGPTCPPE
20 WAALDWSECTPSCGPGLRHRVVLCKSADHRATLPPAHCSPA AKPPATMRCNLRR
PPARWWAGEWGECSAQCGVGQRQSVRCTSH TGQASHECTEALRPPTTTQQCE
AKCDSPTPGDGPEECKDVNKVAYCPLVLKFQFCRAYFRQMCCCKTCQGH

Figure 3. Domain structure of ADAMTS-E and translated nucleic acid sequence. A) Diagram of ADAMTS-E showing the following domains and signature motifs (with amino acid numbers in parentheses): prodomain (1-66), furin cleavage site (63-66), metalloproteinase domain (67-453), zinc-binding motif (392-420), disintegrin domain (469-531), TSP1 motif (548-601), and four TSP1-like motifs (829-884, 888-944, 948-1002, and 1007-1058). Overlapping clones covering the indicated sequence segments are depicted at the bottom of the diagram. **B)** ADAMTS-E nucleotide sequence with translated amino acid sequence above.



B

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1  CACGCGTCCG ACGGCGCGGA GGCCCGGGC GCGGCGCAG AGCCCGGTGA TGCTGCGAAG GCTGTGAACA GGGGAGGGCG
   GTGCGCAGCG TGCCGCGCCT CCGGGGCCCG CGCCGCGTCC TCGGGCCACT ACGACGCTTC CGACACTTGT CCCCTCCGCC
+1                                     M A P A C Q I
                                     =====
81  CACTGTGGGG GCTGCCGGCA GCCGGGGCTG GGGAGAGACA TGTGGACACG TGGCCTCTAT GGCTCCCGCC TGCCAGATCC
   GTGACACCCC CGACGGCCGT CGGCCCGGAC CCCTCTCTGT ACACCTGTGC ACCGGAGATA CCGAGGGCGG ACGGTCTAGG
+1 L R W A L A L G L G L M F E V T H A F R S Q D E F L S
                                     =====
161 TCCGCTGGGC CCTCGCCCTG GGGCTGGGCC TCATGTTGGA GGTCACGCAC GCCTCCGGT CTCAAGATGA GTTCTGTCC
   AGGCGACCCG GGAGCGGGAC CCCGACCCGG AGTACAAGCT CCAGTGCGTG CGGAAGGCCA GAGTTCTACT CAAGGACAGG
+1 S L E S Y E I A F P T R V D H N G A L L A F S P P P P
   Prodomain
   =====
241 AGTCTGGAGA GCTATGAGAT CGCCTTCCCC ACCCGCGTGG ACCACAACGG GGCACGTGCTG GCCTTCTGCG CACCTCCTCC
   TCAGACCTCT CGATACTCTA GCGGAAGGGG TGGGCGCACC TGGTGTTGCC CCGTGACGAC CGGAAGAGCG GTGGAGGAGG

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[illegible]

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+1 R R Q R R G T G A T A E S R L F Y K V A S P S T 4 P
Furin Cleavage Site (Motif)
=====
Prodomain Metalloproteinase Domain
321 CCGAGGAGCAG CGCCGCGGCA CGGGGGCCAC AGCCGAGTCC CGCCTCTTCT ACAAGATGGC CTCGCCGACG AGCCATTTTC
GGCCTCCGTC GCGGCGCGCT GCCCCCGGTG TCGGCTCAGG GCGGAGAAGA TGTTTCACCG GAGCGGGTGC TGGTTPAACG

-1 L L N L T R S S R L L A G H V S V E Y W T R E G L A A
Metalloproteinase Domain
401 TGCTGAACCT GACCCGAGC TCCCGTCTAC TGGCAGGGCA CGTCTCCGTG GAGTACTGGA CACGGGAGGG CCGTGGCTTG
ACGACTTGGA CTGGGCGTCG AGGGCAGATG ACCGTCCCGT GCAGAGGGAC CTCATGACCT GTGCCCTGCC GGACCTGACG

+1 Q R A A R P H C L Y A G H L Q G Q A S T S H V A I S T
Metalloproteinase Domain
481 CAGAGGGCGG CCGGCGCCCA CTGCCCTCTAC GCTGGTCACC TGCAGGGCCA GGGCAGCACC TCCCATGTGG CCATCAGCAC
GTCTCCCGCC GGGCCGGGGT GACGGAGATG CGACCAATGG ACGTCCCGGT CCGGTCGTGG AGGGTACACC GGTAGTCTGG

+1 C G G L H G L I V A D E E E Y L I E P L H G G P K S
Metalloproteinase Domain
561 CTGTGGAGGC CTGCACGGCC TGATCGTGGC AGACGAGGAA GATACCTGA TTGAGCCCTC GCACGGTGGG CCAAGAGGTT
GACACCTCCG GACGTGCGGG ACTAGCACCG TCTGCTCCTT CTCATGGAAT AACTCGGGGA CGTGCCACCC GGGTTCGCAA

+1 S R S P E E S G P H V V Y K R S S L R H P H L D T A T
Metalloproteinase Domain
641 CTCGGAGCCC GGAGGAAAGT GGACCCATGT TGGTGTACAA GGTCTCCTCT CTGCGTCACC CCACCTGTGA CACAGCCTGT
GAGCCTCGGG CCTCCTTTCA CTGGGTGATC ACCACATGTT CGCAAGGAGA GACGCASTGG GGGTGGACCT GTGTGCGACA

+1 G V R D E K P W K G R P W L R T L K P P P A R P L G
Metalloproteinase Domain
721 GGAGTGAGAG ATGAGAAACC GTGAAAGGG CGGCCATGGT GGTGTGGGAC CTGGAAGCCA CCGCTGCCA GGCCTCGTGG
CCTCACTCTC TACTCTTTGG CACCTTTCCC GCGGTACCA CCGACGCTGT GAACCTCGST GCGGAGCGGT CCGGGGACCC

+1 N E T E R G Q P G L K R S V S R E R Y V E T L V V A
Metalloproteinase Domain
801 GAATGAACAA GAGCGTGGCC AGCCAGGCCT GAAGCGATGC GTCAGCCGAG AGCGCTAGCT GGAGACCGTG GTGGTGGCTG
CTTACTTTGT CTGCGACCGG TGGTCCGGA CTTCGCTAGC CAGTCGGCTC TCGGATGCA CCTCTGGGAG CACCAACGAG

+1 D K M M V A Y H G R R D V E Q Y V L A I M N I V A K L
Metalloproteinase Domain
881 ACAAGATGAT GGTGGCCTAT CACGGGCGCC GGGATGTGGA GCAGTATGTC CTGGGCATCA TGAACATTGT TGCCAAACTT
TGTTCTACTA CCACCGGATA GTGCCCGCGG CCTACACCT CGTCATACAG GACCGGTAGT ACTGTGAACA ACGGTTTGG

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-1 F Q D S S L G S T V N I L V T R L I L L T E D Q P T L
Metalloproteinase Domain
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AAGGTCTGTA GCTCAGACCC TTCGTGGCAA TTGTAGGAGC ATTGAGCGGA GTAGGACGAG TGCCCTCTGG TCGGCTGAGG

+1 E I T H H A G K S L D S F C K W Q K S I V N H G L
Metalloproteinase Domain
=====
1041 GGAGATCACC CACCATGCGG GGAAGTCCTT GGACAGCTTC TGTAACTGGC AGAAATCCAT CGTGAACCAAC AGCGGCCATG
CCTCTAGTGG GTGGTACGGC CCTTCAGGGA CCTGTGGAAG ACATTACCGC TCTTTAGGTA GCATCTGGTG TCGCCGGTAC

+1 G N A I P E N G V A N H D T A V L I T R Y D I C I Y K
Metalloproteinase Domain
=====
1121 GCAATGCCAT TCCAGAGAAC GGTGTGGCTA ACCATGACAC TSCAGTGCTC ATCACAGCCT ATGACATCTG CATCTACAPG
CGTTACGGTA AGGTCTCTTC CCACACCGAT TGGTACTGTG TGTACAGAG TAGTGTGCGA TACTGTAGAC GTAGATGTTC

+1 N K P C G T L G L A P V G G M C E R E R S C S V N E D
Metalloproteinase Domain
=====
1201 AACAAACCTT GCGGCACACT AGGCCTGGCC CCGGTGGGCG GAATGTGTGA GCGCGAGAGA AGCTGCAGCG TCAATGAGGA
TTGTTTGGGA CGCCGTGTA TCCGGACCGG GGCACCCGCG CTTACACACT CGCGCTCTCT TCGACGTGCG AGTTACTCCT

+1 I G L A T A F T I A H E I G H T F G M N H D G V G N
Zinc-binding Motif
=====
Metalloproteinase Domain
=====
1281 CATTGGCCCTG GCCACAGCGT TCACCATTGC CCACGAGATC GGGCACACAT TCGGCATGAA CCATGACGGC GTGGGAACA
GTAACCGGAC CGGTGTGCA AGTGGTAACG GGTGCTCTAG CCGGTGTGTA AGCCGTACTT GGTACTGCGG CACCCTTTGT

+1 S C G A R G Q D P A K L M A A H I T M K T N P F V W S
Zinc-binding Motif
=====
Metalloproteinase Domain
=====
1361 GCTGTGGGCG CCGTGGTCAG GACCCAGCCA AGCTCATGGC TGCCACATT ACCATGAAGA CCAACCCATT CGTGTGGTCA
CGACACCCCG GGCACCACTC CTGGTCCGT TCGAGTACCG ACGGTTGTAA TGTACTTCT GGTGGGTAA GCACACCACT

+1 S C S R D Y I T S F L D S G L G L C L N N R P P R Q D
Metalloproteinase Domain
=====
1441 TCCTGCAGCC GTGACTACAT CACCAGCTTT CTAGACTCGG GCCTGGGGCT CTGCCTGAAC AACCGGCCCC CCAGACAGGA
AGGACGTCGG CACTGATGTA GTGGTCGAAA GATCTGAGCC CGGACCCGGA GACGGACTTG TTGGCCGGGG GGTCTGTCTT

+1 F V Y P T V A P G Q A Y D A D E Q C R F Q H G V K S
Disintegrin Domain
=====
1521 CTTTGTGTAC CCGACAGTGG CACCGGGCCA AGCCTACGAT GCAGATGAGC AATGCCGCTT TCAGCATGGA GTCAAATCGC
GAAACACATG GGTGTTCACC GTGGCCCGGT TCGGATGCTA CGTCTACTCG TTACGGCGAA AGTCGTACCT CAGTTTAGCG

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03042403 "0410101"

+1 R Q C K Y G E V C S E L W C L S K S N R C I T N S I P
Disintegrin Domain

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CAGTCACATT TATGCCCTCC CAGACGTCCG TCGACACCAC AGACTCGTTC TCGTTGGCCA CGTAGTGGTT GTCGTAGGCG

+1 A A E G T L C Q T H T I D K G W C Y K R V C V P F S S
Disintegrin Domain

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+1 R P E G V D G A W G P W T P W G D C S R T C G G S V
TSPI Motif

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+1 S S S S R H C D S P R P T I G G K Y C L G E R R R H R
TSPI Motif

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GGAGAGATC GGCAGTGAC CTGTGCGGGT CCGGTTGGTA GCGCCCGTTC ATGACAGACC CACTCTCTTC CGCGCTGCG

+1 S C N T D D C P P G S Q D F R E V Q C S E F D S I P F
TSPI Motif

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AGGACGTTGT GCGTACTGAC AGGGGGACCG AGGGTCTGA AGTCTCTTCA CGTCACAGA CTAAACTCT CGTAGGGAAG

2001 CCGTGGGAAA TTCTACAAGT GGAAAACTGA CCGGGGAGGG GCGGTGAAGG CCGTCTCGCT CAGCTGCCTA GCGGAAGGCT
GGCACCTTT AAGATGTTC CTTTTGCAT GGCCCTCTCC CCGCACTTC GGACGAGCGA GTGCACGGAT CGCCTTCGA

2081 TCAACTTCTA CACGGAGAGG GCGGCAGCCG TGTTGGACGG GACACCCTGC CGTCCAGACA CGTGGACAT TTGCTCAGT
AGTTGAAGAT GTGCCTCTCC CGCGCTCGGC ACCACTCGCC CTGTGGACG GCAGTCTGT GCCACTGTA AACCGAGTCA

2161 GCGGAATGCA AGCAGCTGGG CTGCGACCGA GTCTGGGCT CCGACCTGCG GGAGGACAAG TGCCGAGTGT GTGGCGGTGA
CGCCTACGT TCGTGCACCC GACGCTGGCT CAGGACCCGA GGCTGGACG CCTCTGTTG ACGGCTCACA CACCGCAGT

2241 GSGACETIEGVFSPASPGAGYEDV VWI
CGGCAGTGCC TGCGAGACCA TCGAGGGCGT CTTACGCCCA GCCTCACTGC GGGCCGGGTA CGAGGATGTC GTCTGGATTC
GCGCTACGG ACGCTCTGGT AGCTCCCGCA GAAGTCGGGT CCGAGTGGAC CCGCGCCCAT GCTCTACAG CAGACCTAAG

2321 PKGSVHI F IQD LNL SLS H L A L K G D Q E S
CCAAAGGCTC CGTCCACATC TTCATCCAGG ATCTGAACCT CTCTCTCAGT CACTTGGCCC TGAAGGGAGA CGAGGAGTCC
GTTTCCGAG GCAGGTGTAG AAGTAGGTCC TAGACTTGA GAGAGAGTCA GTGAACCGGG ACTTCCCTCT GTCTCCAGG

2401 L L L E G L P G T P Q P H R L P L A G T T F Q L R Q G
CTGCTGCTGG AGGGGCTGCC CGGGACCCCC CAGCCCCACC GTCTGCTCT AGCTGGGACC ACCTTTCAC TCGCACAGGG
GACGACGACC TCCCCGACGG GCGCTGGGGT GTCGGGGTGG CAGACGGAGA TCGACCTTGG TGAAGATTG ACCTGTCTCC

GenBank accession number: U00001.1

+1 P D Q V Q S L E A L G P I N A S L I V M V L A R T E
 2481 GCCAGACCAG GTCCAGAGCC TCGAAGCCCT GGGACCGATT AATGCATCTC TCATCGTCAT GGTGCTGGCC CGGACCGGCG
CGGTCTGGTC CAGGTCTCGG AGCTTGGGGA CCTTGGCTAA TTACGTAGAG AGTAGCAGTA CCACGACCGG GCGTGGCTGG

+1 L P A L R Y R F N A P I A R D S L P P Y S W H Y A P W
 TSPl-like Motif

2561 TGGCTGCCCT CCGCTACCGC TTCAATGCCC CCATCGCCCG TGA CTGCTG CCGCCCTACT CCGGCACTA TCGGCGCTCG
ACGGACGGGA GCGATGGCG AAGTTACGGG GGTAGCGGC ACTGACGAC GGGGGATGA GGACCTGAT ACGGGGAGCG

+1 T K C S A Q C A G G S Q V Q A V E C R N Q L D S S A V
 TSPl-like Motif

2641 ACCAAGTGCT CGGCCAGTG TGCAGGCGGT AGCCAGGTGC AGGCGGTGGA GTGCCGCAAC CAGCTGGACA GTCGCGGCT
TGGTTACAGA GCGGGTCA CAGTCCGCCA TCGTCCACG TCCGCCACCT CAGGCGTTG GTGACACTGT CAGTGGCTCG

+1 A P H Y C S A H S K L P K R Q R A C N T E P C P P D
 TSPl-like Motif

2721 CGCCCCCAC TACTGCAGTG CCCACAGCAA GCTGCCCAA AGGCAGCGCG CTGCAACAC GGAGCCTTGC CCTCCAGACT
GCGGGGGTGT ATGACGTCAC GGGTCTGCTT CGACGGGTTT TCGTCCGCG GACGTTGTG CCTCGGAACG GGAGGTCTGA

+1 W V V G N W S L C S R S C D A G V R S R S V V C Q R R
 TSPl-like Motif

2801 GGGTTGTAGG GAAGTGTGCG CTCTGCAGCC GCAGCTGCGA TGCAGGCGTG CGCAGCGCT CCGTGTGTG CCAGCGCGCG
CCCAACATCC CTTGACCAGC GAGACGTCGG CGTCGACGCT ACGTCCGAC GCGTCGGCA GCCAGCACAC GGTGCGCGCG

+1 V S A A E E K A L D D S A C P Q P R P P V L E A C H G
 TSPl-like Motif

2881 GTCTCTGCC CGGAGGAGAA GCGGTGGAC GACAGCGCAT GCGCGCAGCC GCGCCACCT GTACTGGAGS CCTGCCACGG
CAGAGACGGC GCCTCTCTT CCGCGACCTG CTGTGCGTA CGGGCTCGG CGCGGTGGA CATGACCTCC GGACGGTSCG

+1 P T C P P E W A A L D W S E C T P S C G P G L R H R
 TSPl-like Motif

2961 CCCCACTTGC CCTCCGGAGT GGGCGGCCCT CGACTGGTCT GAGTGACCC CCAGCTCGCG GCGGGCGCTC CGCCACCGCG
GGGGTGAACG GGAGGCTCA CCGCGCGGA GCTGACCAGA CTCACGTGG GGTGACGCC CGGCCCGGAG GCGGTGGCGC

+1 V V L C K S A D H R A T L P P A H C S P A A K P P A T
 TSPl-like Motif

3041 TGGTCTTTG CAAGAGCGCA GACCACCGCG CCACGCTGCC CCGGCGCAC TGCTACCCG CGGCAAGCC ACCGGGACCG
ACGAGGAAC GTTCTCGCT CTGGTGGCG GGTGCGACGG GGGCGCGTG ACGAGTGGG GCGGTTGCG TGGCGGCTGG

+1 M R C N L R R C P P A R W V A G E W G E C S A Q C G V
 TSPl-like Motif

3121 ATGCGTGCA ACTTGCSCCG GTCCCGCCG GCCCGTGGG TGCGTGCGA GTGGGTGAG TGCTCTGAC AGTGCGCGGT
TACGCGACGT TGAACGCGG GACGGGGGG CGGGCGACCC ACCGACCGCT CACCCACTC ACGAGACGT TCACGCGCGA

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+1  G Q R Q R S V R C T S H T G Q A S H E C T E A L P P
      TSPl-like Motif
=====
3201  CGGGCAGCGG CAGCGCTCGG TGCGCTGCAC CAGCCACAG GGCAGGCGT CGCACGAGTG CACGGAGGCC CTGCGCGCCTC
      GCGCGCTGCC GTCGCGAGCC AGCGCAGCTG GTCGGTGTGC CCGGTCCGCA GCGTGCTCAC GTGCTCCCGG GACGCGCGCG
+1  P T T T Q Q C E A K C D S P T P G D G P E E C K D V N
      TSPl-like Motif
=====
3281  CGACTACCAC GCAGCAGTGT GAGGCCAAGT GCGACAGCCC AACCCCCGGG GACGGCCCTG AAGAGTGCAA GGATGTGAAC
      GCTGATGGTG CGTCGTCACA CTCGGTTCA CGCTGTCGGG TTGGGGGCCC CTGCGGGGAC TTCTACGTT GGTTCGCTG
+1  K V A Y C P L V L K F Q F C S R A Y F R Q M C C F T C
3361  AAGGTCGCTT ACTGCCCCCT GGTGCTCAAA TTTCAGTTCT GCAGCCGAGC CTACTTCCG CAGATGTGCT GCAAAACCTG
      TTCCAGCGGA TGACGGGGGA CCACGAGTTT AAAGTCAAGA CGTCGGCTCG GATGAAGGCG GTCTACACGA GGTTCGGAG
+1  Q G H
3441  CAGGGGCCAC TAGGGGGCGC GCGGCACCCG GAGCCACAGC TGGCGGGGTC TCCGCCGCCA GCCCTGCAGC GGGCCGCGCA
      GGTCCCGGTG ATCCCCCGCG CCGCTGGGCG CTCGGTGTG ACGGCCCCAG AGCGGGCGGT CGGGACGTG CCGGCGCGGT
3521  GAGGGGGCCC CGGGGGGGGC GGGAACTGGG AGGGAAGGCT GAGACGGAGC CGGAAGTTAT TTATTGGGAA CCCCTGCAGG
      CTCCCCCGGG GCGCCCCCGG CCGTTGACCC TCCTTCCCA CTCTGCTCG GCCTTCAATA AATAACCTT GGGGACGTCC
3601  GCCCTGGCTG GGAGGATCCA CCCCACCTC TGCCCTGCC GCGCCAGGGG CACCCGACA TCCAGGCCAC CCGCTCATGG
      CGGGACCGAC CCTCCTAGGT GGGGTTGGAG ACGGGACGGG CCGGGTCCCC GTGGGGCTGT AGGTCCGGTG GGGGAGTACC
3681  TGCTACAGAC CTGCCCCTGG GCGCCACACA CTCCTGCCAG GAAGCCCTAC ATCAATAAAG TTCTGTCTTG TGTAGATTTC
      ACGATGTCTG GGACGGGACC CCGGTGTGT GAGGACGGTC CTCGGGATG TAGTTATTTC AAGACAGAAC ACATCTAAG
3761  TAAAAAAAAA AAAAAA
      ATTTTTTTTT TTTTTT

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Fig. 4

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Metalloproteinase Domain Alignment of ADAMTS-E v. ADAMTS Family

		Percent Homology
	Sim	Ident
ADAMTS-4 (AB014588)	181	
ADAMTS-5 (AF142099)	47	31
ADAMTS-1 (AF060152)	45	31
ADAMTS-6 (AF140674)	51	33
ADAMTS-8 (AF060153)	73	59
ADAMTS-2 (AJ003125)	48	30
E-MPD	49	33
Consensus	63	48
ADAMTS-4 (AB014588)	266	
ADAMTS-5 (AF142099)	266	
ADAMTS-1 (AF060152)	266	
ADAMTS-6 (AF140674)	266	
ADAMTS-8 (AF060153)	266	
ADAMTS-2 (AJ003125)	266	
E-MPD	266	
Consensus	266	
ADAMTS-4 (AB014588)	351	
ADAMTS-5 (AF142099)	351	
ADAMTS-1 (AF060152)	351	
ADAMTS-6 (AF140674)	351	
ADAMTS-8 (AF060153)	351	
ADAMTS-2 (AJ003125)	351	
E-MPD	351	
Consensus	351	
ADAMTS-4 (AB014588)	436	
ADAMTS-5 (AF142099)	436	
ADAMTS-1 (AF060152)	436	
ADAMTS-6 (AF140674)	436	
ADAMTS-8 (AF060153)	436	
ADAMTS-2 (AJ003125)	436	
E-MPD	436	
Consensus	436	
ADAMTS-4 (AB014588)	521	
ADAMTS-5 (AF142099)	521	
ADAMTS-1 (AF060152)	521	
ADAMTS-6 (AF140674)	521	
ADAMTS-8 (AF060153)	521	
ADAMTS-2 (AJ003125)	521	
E-MPD	521	
Consensus	521	

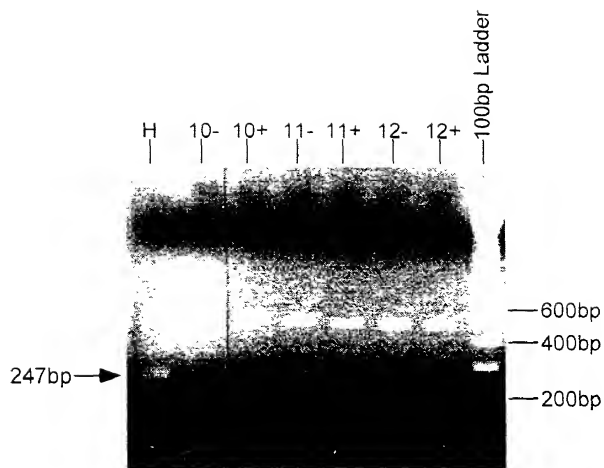


Figure 5. Expression of ADAMTS-E in cDNA from osteoarthritic cartilage.

Figure 6. Amino acid alignment of human ADAMTS-E with a GenScan prediction of ADAMTS-E from mouse genomic sequence.

hADAMTS-E	(1)	1-----HASDGAEPGAAQEPG--DAAKAVNRGGGTVGAAASRGWGETCGHVASMAPACQILRWALALG	20
mADAMTS-E	(2)	XMCDHSSYSPFPVLLRLRVGNGCQLPHKVDVKGTSDAAQTNRGGSTVGAAASRGWGETCGHVAFMASACQILRWALALG	
Consensus	(1)	G P G DAA VNRGG TVGAA SRGWGETCGHVA MA ACQILRWALALG	
hADAMTS-E	(62)	81LGLMFVETHAFRSQDEFLSSLESYEIAFPTRVDHNGALLAFSPPPRRQRRTGATAESRLFYKVASPSTHFLNLTPSS	160
mADAMTS-E	(81)	LGLTFKVTHAFRSQDELLSSLESYEIAFPTRVDHNGAMLAFSPPAATRRQRAGAGATTESRLFYKVASPSTHFLNLTPSS	
Consensus	(81)	LGL F VTHAFRSQDE LSSLESYEIAFPTRVDHNGA LAFSP RQRRG GAT ESRFYKVA PSTHFLNLTPS	
hADAMTS-E	(142)	161RLLAGHVSVVEYWTREGLAWQRAARPHCLYAGHLQQAQSTSHVAISTCGGLHGLIVADEEYVLEIPLGGKPKGSRSPSEESG	241
mADAMTS-E	(161)	RLLAGHVSVVEYWTREGLAWQRAARHCLYAGHLQQAQSSHVAVSTCGGLHGLIVADEEYVLEIPLQGPKGHRGPEESG	
Consensus	(161)	RLLAGHVSVVEYWTREGLAWQRAAR HCLYAGHLQQA SHVA STCGGLHGLIVAD EEVYLEIPL GPKG R PEESG	
hADAMTS-E	(222)	241PHVVYKRSSLRHPHLDTACGVRDEKPKWGRPWMLRTLKPPPARPLGNETERGQPLKRSVSRERYVETLVADKMMVAH	320
mADAMTS-E	(241)	PHVVYKRSSLRHPHLDTACGVRDEKPKWGRPWMLRTLKPPPARPLGNESERGQLKRSVSRERYVETLVADKMMVAH	
Consensus	(241)	PHVVYKRSSLRHPHLDTACGVRDEKPKWGRPWMLRTLKPPPARPLGNE ERGQ GLKRSVSRERYVETLVADKMMVAH	
hADAMTS-E	(302)	321GRRDVEQVYLAIMNV-----AKLFQDSSSLGSTVNILVTRLILLTDEQPTLEITHHAGKSLDSFCWKQKSI VNSH	400
Consensus	(321)	GRRDVEQVYLAIMNITRSLFLGGQVAKLFDQSSLGNIVNIVLTRLILLTDEQPTLEITHHAGKSLDSFCWKQKSI VNSH	
hADAMTS-E	(372)	401GHGNAIPENGVAHNHTAVLITRYDICIYKNKPCGTLGLAPVGGMCERERSCSVNEDIGLATAFTIAHEIGHTFGMNHGCV	480
mADAMTS-E	(401)	GHGNAIPENGVAHNHTAVLITRYDICIYKNKPCGTLGLAPVGGMCERERSCSNEDIGLATAFTIAHEIGHTFGMNHGCV	
Consensus	(401)	GHGNAIPENGVAHNHTAVLITRYDICIYKNKPCGTLGLAPVGGMCERERSCS NEDIGLATAFTIAHEIGHTFGMNHGCV	
hADAMTS-E	(452)	481GNSCGARGQDPAKLMAAHITMKTNPFVWSSCSRDIYITSLDSSLGLCLNNRPPRQDFVYPTVAPGQAYDADEQCQRFQHG	560
mADAMTS-E	(481)	GNSCGARGQDPAKLMAAHITMKTNPFVWSSCSRDIYITSLDSSLGLCLNNRPPRQDFVYPTVAPGQAYDADEQCQRFQHG	
Consensus	(481)	GN CGARGQDPAKLMAAHITMKTNPFVWSSCSRDIYITSLDSSLGLCLNNRPPRQDFVYPTVAPGQAYDADEQCQRFQHG	
hADAMTS-E	(532)	561KSRQCKYGEVCSSELWCLSKSNRCITNSIPAAEGTLCQTHITDKGWCKYKRVCPFGSRPEGVDGAWGPWTPWGDSCSRCCG	640
mADAMTS-E	(561)	KSRQCKYGEVCSSELWCLSKSNRCITNSIPAAEGTLCQTHITDKGWCKYKRVCPFGSRPEGVDGAWGPWTPWGDSCSRCCG	
Consensus	(561)	KSRQCKYGEVCSSELWCLSKSNRCITNSIPAAEGTLCQTHITDKGWCKYKRVCPFGSRPEGVDGAWGPWTPWGDSCSR CGG	
hADAMTS-E	(612)	641GVSSSSRHCDSPRPTIGGKYCLGERRRRHSNCNTDDCPFGSQDFREYQCSFEFDSIPFRGKFYKWTYRGGGVKACSLTCLA	720
mADAMTS-E	(641)	GVSSSSRHCDSPRPTIGGKYCLGERRRRHSNCNTDDCPFGSQDFREYQCSFEFDSIPFRGKFYKWTYRGGGVKACSLTCLA	
Consensus	(641)	GVSSSSRHCDSPRPTIGGKYCLGERRRRHSNCNT DCPFGSQDFRE YQCSFEFDS IPFRGKFY KWTYRGGGVKACSLTCLA	
hADAMTS-E	(692)	721EGFNFYTERAAAVVDGTPCRPDTVDICVSGECKHVGCDDVLSGLDREDKRCVCGDGSACETIEGVFSPASPAGAYEDVV	800
mADAMTS-E	(721)	EGFNFYTERAAAVVDGTPCRPDTVDICVSGECKHVGCDDVLSGLDREDKRCVCGDGSACETIEGVFSPASPAGAYEDVV	
Consensus	(721)	EGFNFYTERAAAVVDGTPCRPDTVDICVSGECKHVGCDDVLSGLDREDKRCVCGDGSACETIEGVFSPA PG GYEDVV	
hADAMTS-E	(772)	801WIPKGSVHIETQDLNLSLSHLALKGQESLLEGLPGTPQPHRLPLAGTTTFLRQGPQVQSLALGPINASLIVMLAR	880
mADAMTS-E	(801)	WIPKGSVHIETQDLNLSLSHLALKGQESLLEGLPGTPQPHRLPLAGTTTFLRQGPQVQSLALGPINASLIMVLAQ	
Consensus	(801)	WIPKGSVHIETQDLNLSLSHLALKGQESLLEGLPGTPQPHRLPLAGTTT LRQGPQV QSLALGPINASLI MVLA	
hADAMTS-E	(852)	881TELPALRYRFNAPIARDLPPYSWHYAPWTKCSAQAGGSQVQVVECRNQDSSAVAPHYCSAHSKLPKRQRACNTEPCP	960
mADAMTS-E	(881)	AELPALHYRFNAPIARDLPPYSWHYAPWTKCSAQAGGSQVQVVECRNQDSSAVAPHYCSGHSKLPKRQRACNTEPCP	
Consensus	(881)	ELPAL YRFNAPIARD LPPYSWHYAPWTKCSAQAGGSQVQ VECRNQDSSAVAPHYCS HSKLPKRQRACNTEPCP	
hADAMTS-E	(932)	961PDWVVGWNSLCSRSCDAGVRSRVVCQRRVSAAEEKALDSDACQPPRPVLEACHGFTCPPEWALDWSSECTPSCGPGLR	1040
mADAMTS-E	(961)	PDWVVGWNSRCSRSCDAGVRSRVVCQRRVSAAEEKALDSDACQPPVLEACHGFTCPPEWALDWSSECTPSCGPGLR	
Consensus	(961)	PDWVVGWNS CSRSCDAGVRSRVVCQRRVSAAEEKALDSDACQPPRPVLEAC GP CPPEWA LDWSSECTPSCGPGLR	

